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Population-Based Cancer Survival (2001 to 2009) in the United States: Findings From the CONCORD-2 Study

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CONFLICT OF INTEREST DISCLOSURES

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INTRODUCTION

In this supplement to *Cancer*, we provide survival estimates by race (black vs white), state of residence at the time of diagnosis, and stage of disease at the time of diagnosis for 9 solid tumors in men and women [1–9] and for acute lymphoblastic leukemia in children.[10] Data are from 37 statewide cancer registries that participated in the CONCORD-2 study,[11] covering approximately 80% of the US population. Each of the 10 cancer-specific articles includes clinical and cancer control perspectives. These perspectives highlight how clinical practice may have had an impact on population-based cancer survival trends, and how states funded by the Centers for Disease Control and Prevention (CDC)'s National Comprehensive Cancer Control Program[12] can use population-based survival data, along with incidence and mortality data, to inform cancer control activities.[13]

The Growing Cancer Burden

Cancer may soon become the leading cause of death in the United States: it is already the leading cause in nearly one-half of all states.[14] Although the risk of dying of cancer continues to decrease, as measured by the age-standardized death rate, the actual number of cancer deaths continues to increase.[15] This increase is being driven to a large extent by demographic trends related to a growing and aging US population. By 2020, nearly 2 million men, women and children and children will be diagnosed with cancer annually.[16] In addition, the number of individuals living with and after a cancer diagnosis (cancer survivors) also will increase from an estimated 14 million in 2012 to 18 million by 2022.[17] Cancer survivors remain at risk of recurrence of their cancer, the development of subsequent new cancers, and side effects related to their cancer treatment.[18]

The prevention of many of these cancers is possible through behavioral, environmental, policy, and clinical interventions to address the wide range of factors that put individuals at increased risk of developing cancer over their lifetime.[19] However, even if all known effective strategies for cancer prevention were broadly implemented today, the impact on cancer incidence would likely not be observed for several decades due to the long latency period for many cancers. The anticipated increase in the number of new patients with cancer and survivors poses an enormous challenge for the US health care system to meet the need to screen, diagnose, and treat these individuals.[20,21] It also is a major challenge to the public health community to help patients with cancer meet the financial, physical, and psychological challenges related to their cancer experience, including difficulties in returning to full economic activity.[22,23]

To address the challenge of the growing cancer burden, the CDC's Division of Cancer Prevention and Control collaborates with state and national partners to implement public health strategies to promote primary prevention, cancer screening, early diagnosis, and access to effective evidence-based treatment and survivorship care plans.[12] The challenge for the public health community is to put in place primary prevention and early detection strategies for the general population while meeting the growing needs of patients with cancer and cancer survivors.

Cancer Surveillance in the United States

In the United States, cancer control activities primarily take place at the state and local levels, and cancer control planners need information regarding the unique cancer burden in their states. Cancer is the only reportable chronic disease in the country for which there is nationwide surveillance.[24] There currently is a population-based cancer registry in all 50 states and the District of Columbia.[12] In addition to state support, these registries receive federal support from the CDC's National Program of Cancer Registries (NPCR) and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program. These registries provide a census of all individuals diagnosed with cancer and, along with state vital records offices, collect and report a basic set of information concerning all new cancer cases (incidence), deaths (including those caused by cancer), the number of patients with cancer alive in a given calendar period (prevalence), and the probability of being alive up to a given point in time after diagnosis (survival).

Population-based cancer survival differs in a fundamental way from the survival of patients with cancer who are participating in clinical trials.[25,26] Population-based survival reflects the average survival for all patients with cancer in the population, regardless of their age, sex, race, health status, stage of disease, socioeconomic position, residence at the time of diagnosis, and access to care. As such, population-based cancer survival provides an indicator of the overall effectiveness of the health care system to deliver screening, early diagnosis, and evidenced-based treatment services and follow-up care to all individuals in the population being served.[25–27]

The CONCORD Programme

The CONCORD Programme at the London School of Hygiene and Tropical Medicine established worldwide surveillance of population-based cancer survival in 2015.[11,25] The first CONCORD study provided a systematic comparison of survival for patients aged 15 to 99 years who were diagnosed with a cancer of the female breast, colon, rectum, or prostate between 1990 and 1994.[28] International differences in 5-year age-standardized survival were wide, even after adjustment for differences in mortality from other causes of death. Survival in the United States was among the highest in the world. However, the study reported large and consistent black and white racial disparities in survival for all 4 cancers in the United States (Table 1).[11,28,29] For example, survival T1 for black women diagnosed with breast cancer was 14% lower than that for white women and ranked, along with breast cancer survival in the United Kingdom, just above survival in Eastern European countries but lower than survival in Northern and Western European countries.

The CONCORD-2 study estimated long-term survival trends among 25.7 million individual patients with cancer in 67 countries who were diagnosed during the 15year period between 1995 and 2009 with 1 of 10 common cancers (stomach, colon, rectum, liver, lung, female breast, cervix, ovary, prostate, and leukemia [including children]).[11] As reported in the first CONCORD study, international differences in age-standardized survival were wide, even after adjustment for differences in mortality from other causes of death. Survival in the United States for most cancers again was among the highest in the world.

The cancer survival estimates presented in the 10 cancer-specific articles included in this supplement come from more detailed analysis of the data contributed to the CONCORD-2 study.[11] A description of the data from the 37 participating cancer registries, and the rigorous and advanced statistical methods used to evaluate and analyze the data, are presented in an accompanying article by Allemani et al.[29] We focused on patients diagnosed during 2 calendar periods (2001–2003 and 2004–2009) because the method used by US cancer registries to collect and report anatomic stage (SEER Summary Stage 2000) changed beginning on January 1, 2004. We observed 5-year survival to be high (≥80%) for breast cancer in women,[6] prostate cancer,[9] and acute lymphoblastic leukemia (ALL) in children[10]; moderate (50%-80%) for cancers of the colon,[3] rectum,[2] and cervix[7]; and low (<50%) for cancers of the stomach,[1] liver,[4] lung,[5] and ovary[8] (Table 1).[11,28,29] These observations are consistent with those of long-term trends in survival in the United States for many leading cancers in both males and females and children.[30] The comparison of survival by calendar period in the cancerspecific articles in this supplement shows that even over this relatively short time period, survival has improved for cancers that were highly lethal (stomach,[1] liver,[4] lung,[5] and ovary[8]). However, less progress was observed for cancers for which survival already was moderate to high, likely reflecting previous gains achieved from screening (colon,[3] rectum,[2] breast,[6] and cervix[7]) or those for which treatment already was highly effective (ALL).[10] The high survival for patients with prostate cancer likely reflects the use of the prostate-specific antigen test for the early detection of cancer, which was recommended by the American Cancer Society during this time period.[31] The potential impact of overdiagnosis also was evident in these data, in which 5year survival after a diagnosis of locally staged prostate cancer in black and white men[9] and breast cancer in white women[6] was close to 100%.

However, as the results from this supplement also demonstrate, the large racial disparities in cancer survival between blacks and whites in the United States are consistent across most 37 states participating in the CONCORD-2 study, and they persisted over time (Table 1).[11,28,29] With the exception of stomach cancer, 5-year survival was lower in black men and women than white men and women for all solid tumors examined. The funnel plots in the accompanying articles for female breast,[6] colon,[3] and ovarian[8] cancers show just how large and consistent these disparities were across the 37 states.

Each of the accompanying articles contains bar charts of 5-year survival for all races combined for each state and each calendar period, grouped by US Census region. Some patterns of regional variation were observed. Survival in several Northeastern states tended to be somewhat higher than the pooled US estimate, whereas survival in several of the Southern states tended to be somewhat lower than the pooled US estimate. As expected, some variation in survival among the states was observed, most likely due at least in part to racial and socioeconomic disparities.

Findings from these analyses may help to explain why net survival in the United States is among the highest of all high-income countries, as reported in both the first CONCORD study and the CONCORD-2 study. The overall high percentage of microscopically verified cancers observed for all cancers,[29] and the relatively low percentage of patients with solid tumors for whom stage at diagnosis was unknown,[1-9] suggests that detailed clinical

investigation at the time of diagnosis was performed for the majority of patients with cancer diagnosed during this time period. However, the large and consistent racial disparities described herein are likely due to the fact that cancers diagnosed in black men and women tended both to be diagnosed at a later stage and to have lower survival at each stage of diagnosis.[1-9] These disparities often appeared within the first year after diagnosis, suggesting that additional factors, such as comorbidities and socioeconomic factors related to limited access to screening, diagnosis, treatment, and follow-up care, may be relevant.

How These Data Can Be Used by Cancer Control Programs

Population-based survival data have been used to plan and evaluate national cancer control strategies in the United Kingdom.[32,33] In the United States, these data can be used by state-based programs to help target and evaluate cancer control strategies promoting screening (colon, rectum, cervical, and breast)[12] and symptom awareness for gynecologic cancers (ovary).[34] It should be noted that survival for women diagnosed with localized ovarian cancer also is high,[8] and future research that focuses on the development of new methods or modalities to detect these cancers while they are still at a local stage may well improve survival for women with ovarian cancer. For cancers with low survival (stomach, liver, lung, and ovary), efforts directed at reducing cancer incidence through primary prevention, when such strategies exist, are likely to have the greatest impact on reducing the cancer burden in the longer term.

Between the first CONCORD study (1990–1994) and the CONCORD-2 study (1995–2009), survival in the United States improved for female breast, colon, rectum, and prostate cancers (Table 1).[11,28,29] However, 5year survival for cancers of the colon diagnosed among black men and women between 2004 and 2009 had yet to reach the levels of survival noted for white men and women diagnosed between 1990 and 1994, some 10 to 15 years earlier. Similar findings were observed for breast cancer in women and rectal cancer in men, for which survival in black patients lagged approximately 15 years behind that for white patients. If equal access to medical care, including screening, diagnosis, and treatment services, yields equal outcome, regardless of race,[35-37] these disparities represent a large number of potentially avoidable premature deaths which, in turn, impose a large economic burden on affected communities.[38]

The findings of large, consistent, and persistent racial disparities in survival should compel robust action. Results from the first CONCORD study demonstrated that breast cancer survival in the United Kingdom was lower than in comparable European countries. This prompted the Department of Health in England to initiate the International Cancer Benchmarking Partnership study with the aim of examining international variations in cancer survival for several leading cancers, and to inform health policy to improve cancer survival through an examination of population awareness and beliefs regarding cancer; attitudes, behaviors, and systems in primary care; delays in diagnosis and treatment and their causes; and treatment, comorbidities, and other factors.[39-42] A similar comprehensive and coordinated initiative at the local and state level in the United States might help to identify the strategies and actions needed to achieve the highest possible survival for all men and

women diagnosed with cancer, regardless of their race, ethnicity, and socioeconomic position.

Strengths and Limitations

There are inherent strengths and limitations in studies performed using data from population-based cancer registries. The high quality and completeness of the US data, and the rigor of the analytic methods used, ensured that the survival estimates reported in this supplement are directly comparable between participating states. In the United States, all cancer registries are members of the North American Association of Central Cancer Registries (NAACCR) and they collect and report incidence data using common procedures and the same data dictionary.[12] The CONCORD-2 study maximized the comparability of the results by using a common protocol for data submission, with standardized quality control procedures and centralized analysis, including advanced statistical methods and the construction of state-specific, race-specific, and sexspecific life tables of all-cause mortality by single year of age and single calendar year, to correct for differences in background mortality. All participating registries met NAACCR certification criteria with respect to the completeness and quality of their incidence data, including ascertainment of cases. Therefore, the findings do not reflect case ascertainment bias wherein patients with a very poor prognosis and shorter survival (eg, those with advanced disease, clinical diagnosis) are less completely captured by the cancer registries than patients with a good prognosis and longer survival.

Several limitations could impact the interpretation of the findings. Although survival data have been shown to be comparable when death ascertainment is complete,[43] follow-up procedures among cancer registries in the United States differ depending on the federal funding source.[12] SEER registries are required to conduct active follow-up of all registered cases to ascertain vital status whereas NPCR registries are only funded to conduct linkage with their state vital records to obtain information regarding deaths that occurred within their state and with the CDC's National Death Index to obtain information concerning deaths that occurred anywhere within the United States. As a result, NPCR registries may miss some deaths, particularly among patients who leave the United States between the time of their diagnosis and death, and slightly overestimate the patient's survival time.[44] This limitation may account for the somewhat higher survival estimates for several large (population) NPCR registries, which were most evident in the funnel plots of highly fatal cancers for which missing deaths could lead to an overestimation of survival.[45] Second, this was the first opportunity for several NPCR registries to collect and report survival data, which may account for some of the state variability observed, particularly in the first (2001–2003) calendar period. The reluctance of some medical facilities to report social security numbers and complete dates of birth to their state cancer registry may have impeded a registry's ability to identify deaths through subsequent linkages with state and national death certificate files. Third, the manner in which SEER Summary Stage 2000 data were collected and reported changed for all registries in 2004. The impact of this change was most evident among NPCR-funded registries, which coded stage data manually in the first calendar period (2001–2003) and then derived stage data in the second calendar period (20042009); the percentage of cases with unknown stage decreased slightly beginning around 2004. Last,

analyses of survival by race were restricted to whites and blacks individuals, the 2 major racial groups in the United States, because life tables for other races and Hispanics were not available.

Future Plans

The CONCORD-3 study currently is in progress. It will update worldwide surveillance of cancer survival trends to include patients diagnosed through 2014.[26] CONCORD-3 will include 15 malignancies that collectively represent approximately 75% of the global cancer burden: esophagus, stomach, colon, rectum, liver, pancreas, lung, melanoma, breast (women), cervix, ovary, and prostate in men and women aged 15 to 99 years and brain tumors, lymphomas, and leukemias in both adults and children aged 0 to 14 years. The US contribution is expected to cover 44 states and up to 90% of the national population.

Conclusions

The quality of the CONCORD-2 data, the rigorous statistical methods used, and the large population coverage provide a broad and comprehensive overview of trends in survival among patients with cancer diagnosed up to 2009. These data provide a valuable contribution to public health and cancer control in the United States and benchmark the status of population-based cancer survival immediately before the implementation of the Patient Protection and Affordable Care Act in 2010. Further improvements in survival may result from collaborations with state and national partners to implement public health strategies to promote cancer screening, early diagnosis, access to effective evidence-based treatment (including personalized cancer care and targeted therapies), and follow-up care. CDC's Division of Cancer Prevention and Control can help to improve access to timely diagnosis and treatment through its screening programs, awareness campaigns, and by facilitating the implementation of long-term survivorship care plans.[12]

The challenge will be to ensure that each individual diagnosed with cancer in the United States benefits equally from advances in diagnosis and treatment.

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Table 1.

Five-Year, Age-Standardized, Population-Based Survival (%) by Calendar Period of Diagnosis, Cancer Site, and Race (Black Versus White)

		CONCORD (1990 to 1994)[a]			CONCORD-2 (2004 to 2009)[b]		
Site	**Sex**	**Black**	**White**	**Difference**	**Black**	**White**	**Difference**
Stomach	Both	NA	NA	NA	28.3	28.0	**0.3**
Colon	Males	51.5	60.5	**−9.0**	54.5	64.5	**−10.0**
	Females	51.0	60.8	**−9.8**	58.6	66.5	**−7.9**
Rectum	Males	47.4	57.3	**−9.9**	53.6	62.8	**−9.2**
	Females	49.4	60.4	**−11.0**	61.8	66.2	**−4.4**
Liver	Both	NA	NA	NA	11.4	14.3	**−2.9**
Lung	Both	NA	NA	NA	14.9	19.4	**−4.5**
Breast	Females	70.9	84.7	**−13.8**	78.4	89.7	**−11.3**
Cervix	Females	NA	NA	NA	55.5	63.5	**−8.0**
Ovary	Females	NA	NA	NA	31.1	41.7	**−10.6**
Prostate	Males	85.8	92.4	**−6.6**	92.7	96.9	**−4.2**
ALL (children)	Both	NA	NA	NA	83.6	88.6	**−5.0**

Abbreviations: ALL, acute lymphoblastic leukemia; NA, not available.

[a]Relative survival; Source: Coleman MP, Quaresma M, Berrino F, et al; CONCORD Working Group. Cancer survival in five continents: a worldwide populationbased study (CONCORD). Lancet Oncol. 2008;9:730–756.[28]

[b]Net survival; Sources: Allemani C, Weir HK, Carreira H, et al; CONCORD Working Group. Global surveillance of cancer survival 1995–2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet. 2015;385:977–101011; and Allemani C, Harewood R, Johnson CJ, et al. Population-based cancer survival in the US: data, quality control and statistical methods. Cancer. 2017;123:000–000.[29]